

## WEST Search History

DATE: Tuesday, September 16, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ</i>			
L6	L5 and tear secretion	20	L6
L5	L4 and lacrimal	62	L5
L4	l1 and dry eye	158	L4
L3	((eye/ )!.IPC.  (dry/ )!.IPC.  (and/ )!.IPC.  (l1/ )!.IPC. )	0	L3
<i>DB=USPT; PLUR=YES; OP=ADJ</i>			
L2	L1	1502	L2
L1	((514/47  514/50  514/51  514/912 )!.CCLS. )	1502	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 09:30:26 ON 16 SEP 2003)

FILE 'CAPLUS, MEDLINE, USPATFULL, EUROPATFULL' ENTERED AT 09:30:43 ON 16 SEP 2003

FILE 'REGISTRY' ENTERED AT 09:30:49 ON 16 SEP 2003

L1	STRUCTURE UPLOADED
L2	1 S L1 SSS SAM
L3	33 S L1 SSS FULL

FILE 'CAPLUS, MEDLINE, USPATFULL' ENTERED AT 09:41:19 ON 16 SEP 2003

L4	69 S L3
L5	20 S L4 AND DRY EYE
L6	9 S L5 AND LACRIMAL

L6 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:300880 CAPLUS

DOCUMENT NUMBER: 138:297704

TITLE: Methods for treating **dry eye** by administering fixed combinations of MUC-1 secretagogues and **lacrimal** gland stimulants

INVENTOR(S): Yanni, John M.; Gamache, Daniel A.

PATENT ASSIGNEE(S): Alcon, Inc., Switz.

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

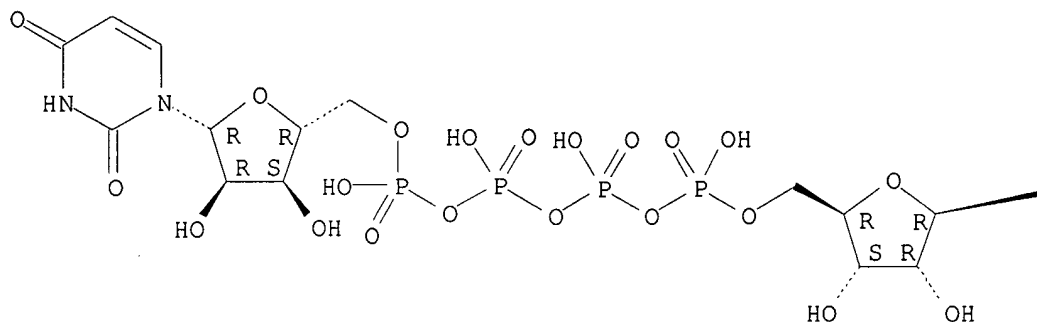
FAMILY ACC. NUM. COUNT: 1

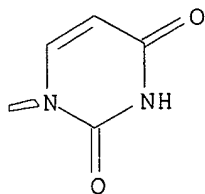
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003030892	A1	20030417	WO 2002-US30673	20020926
W: AU, BR, CA, CN, JP, KR, MX, PL, US, ZA				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
US 2003109488	A1	20030612	US 2002-255205	20020926
PRIORITY APPLN. INFO.:			US 2001-328692P	P 20011011
OTHER SOURCE(S):	MARPAT 138:297704			
AB	Methods of treating <b>dry eye</b> by administering fixed combinations of MUC-1 secretagogues, such as HETE derivs., and <b>lacrimal</b> gland stimulants are disclosed.			
IT	211427-08-6			
	RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(methods for treating <b>dry eye</b> by administering fixed combinations of MUC-1 secretagogues and <b>lacrimal</b> gland stimulants)			
RN	211427-08-6 CAPLUS			
CN	Uridine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with uridine, tetrasodium salt (9CI) (CA INDEX NAME)			

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN  
 ACCESSION NUMBER: 1998:548515 CAPLUS  
 DOCUMENT NUMBER: 129:180137  
 TITLE: Method of treating **dry eye** disease  
 with purinergic receptor agonists  
 INVENTOR(S): Yerxa, Benjamin R.; Jacobus, Karla M.; Pendergast,  
 William; Rideout, Janet L.  
 PATENT ASSIGNEE(S): Inspire Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 41 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 8  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834593	A1	19980813	WO 1998-US2701	19980206
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5900407	A	19990504	US 1997-797472	19970206
AU 9863241	A1	19980826	AU 1998-63241	19980206
AU 735684	B2	20010712		
ZA 9800979	A	19990219	ZA 1998-979	19980206
EP 1003474	A1	20000531	EP 1998-907434	19980206
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2001504858	T2	20010410	JP 1998-535054	19980206
BR 9809562	A	20011002	BR 1998-9562	19980206
NO 9903777	A	19991005	NO 1999-3777	19990804
US 2002065244	A1	20020530	US 2001-10055	20011109
US 2002193340	A1	20021219	US 2001-27520	20011219
US 2002103157	A1	20020801	US 2002-41826	20020103
PRIORITY APPLN. INFO.:			US 1997-797472	A2 19970206
			WO 1998-US2701	W 19980206
			US 1998-171169	A1 19981014

OTHER SOURCE(S): MARPAT 129:180137

AB A method and prepn. for the stimulation of tear secretion in a subject in need of such treatment is disclosed. The method comprises administering to the ocular surfaces of the subject a purinergic receptor agonist such as UTP, dinucleotides, CTP, ATP, or their therapeutically useful analogs

and derivs., in an amt. effective to stimulate tear fluid secretion and enhance drainage of the **lacrimal** system. Pharmaceutical formulations and methods of making the same are also disclosed. Methods of administering the same would include: topical administration via a liq., gel, cream, or as part of a contact lens or selective release membrane; or systemic administration via nasal drops or spray, inhalation by nebulizer or other device, oral form (liq. or pill), injectable, intra-operative instillation or suppository form. P1,P4-di(uridine tetraphosphate) tetrasodium salt (I) was formulated as an isotonic aq. soln. and topically administered to the eyes of rabbits; I at 0.5, 5.0, and 8.5 % concn. significantly increased tear secretion.

IT 211427-07-5 211427-08-6 211427-11-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

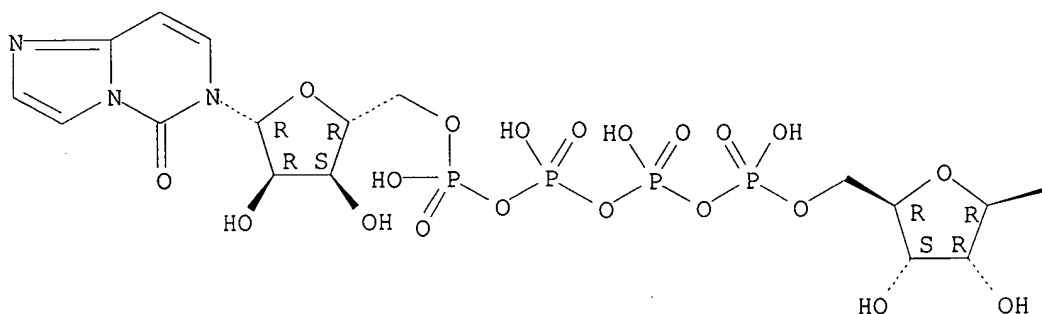
(dry eye disease treatment with purinergic receptor agonists)

RN 211427-07-5 CAPLUS

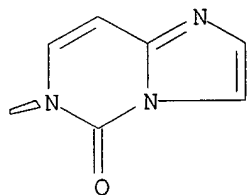
CN Imidazo[1,2-c]pyrimidin-5(6H)-one, 6-[5-O-[hydroxy[[hydroxy[[hydroxy(phosphonoxy)phosphinyl]oxy]phosphinyl]oxy]phosphinyl]-.beta.-D-ribofuranosyl]-, P'''-fwdarw.5'-ester with 6-.beta.-D-ribofuranosylimidazo[1,2-c]pyrimidin-5(6H)-one (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

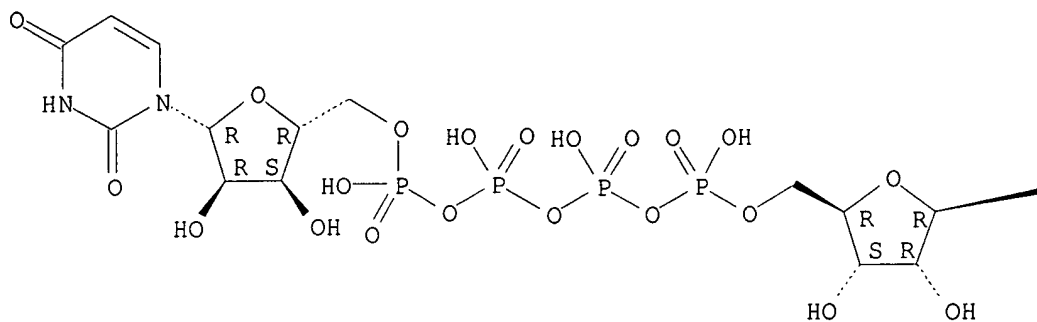


RN 211427-08-6 CAPLUS

CN Uridine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with uridine, tetrasodium salt (9CI) (CA INDEX NAME)

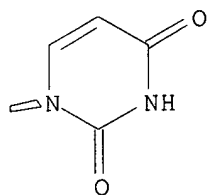
Absolute stereochemistry.

PAGE 1-A



●4 Na

PAGE 1-B

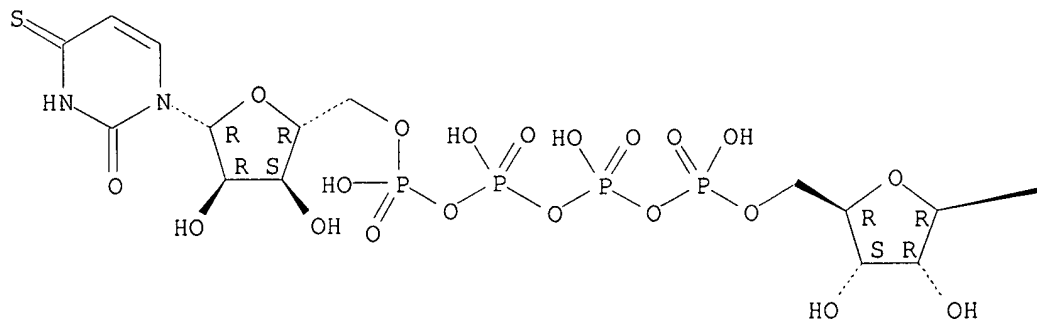


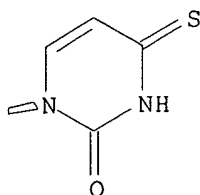
RN 211427-11-1 CAPLUS

CN Uridine 5'-(pentahydrogen tetraphosphate), 4-thio-, P'''-fwdarw.5'-ester with 4-thiouridine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2003:159873 USPATFULL

TITLE: Methods for treating **dry eye**

INVENTOR(S): Yanni, John M., Burleson, TX, UNITED STATES

Gamache, Daniel A., Arlington, TX, UNITED STATES

PATENT ASSIGNEE(S): Alcon, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003109488	A1	20030612
APPLICATION INFO.:	US 2002-255205	A1	20020926 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-328692P	20011011 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Alcon Research, Ltd., Patrick M. Ryan(Q-148), R&D Counsel, 6201 South Freeway, Fort Worth, TX, 76134-2099	
NUMBER OF CLAIMS:	16	
EXEMPLARY CLAIM:	1	
LINE COUNT:	894	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of treating **dry eye** by administering fixed combinations of MUC-1 secretagogues, such as HETE derivatives, and **lacrimal** gland stimulants are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

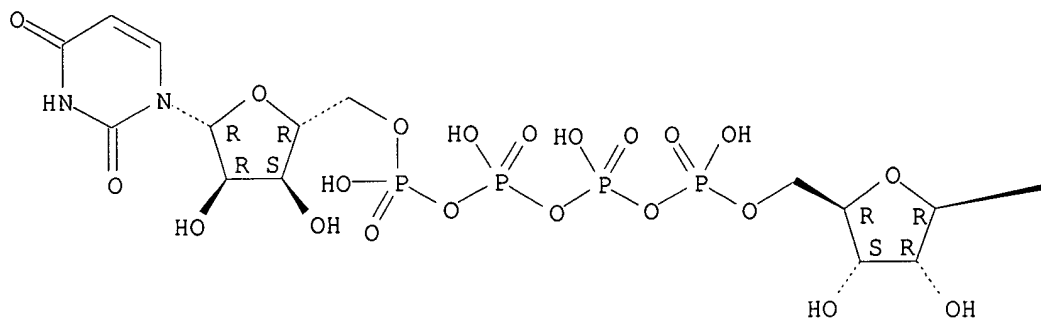
IT 211427-08-6

(methods for treating dry eye by administering fixed combinations of MUC-1 secretagogues and lacrimal gland stimulants)

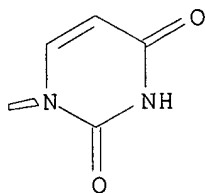
RN 211427-08-6 USPATFULL

CN Uridine 5'-(pentahydrogen tetrphosphate), P''''.fwdarw.5'-ester with uridine, tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 4 Na



L6 ANSWER 4 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2002:337975 USPATFULL

TITLE: Method of treating **dry eye** disease  
with purinergic receptor agonistsINVENTOR(S): Yerxa, Benjamin R., Raleigh, NC, UNITED STATES  
Jacobus, Karla, Cary, NC, UNITED STATES  
Pendergast, William, Durham, NC, UNITED STATES  
Rideout, Janet L., Raleigh, NC, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002193340	A1	20021219
APPLICATION INFO.:	US 2001-27520	A1	20011219 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-171169, filed on 14 Oct 1998, PENDING A 371 of International Ser. No. WO 1998-US2701, filed on 6 Feb 1998, UNKNOWN A 371 of International Ser. No. US 1997-797472, filed on 6 Feb 1997, GRANTED, Pat. No. US 5900407		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	HOWREY SIMON ARNOLD & WHITE, LLP, BOX 34, 301 RAVENSWOOD AVE., MENLO PARK, CA, 94025		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Page(s)		
LINE COUNT:	1124		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			



AB This invention is directed to a method of stimulating tear secretion and mucin production in eyes. The method comprises the step of administering to the eyes of a subject a composition comprising a compound of Formula I, II, III, or IV and its pharmaceutically acceptable salts, in an amount effective to stimulate tear fluid secretion. The method of the present invention may be used to increase tear production for any reason, including, but not limited to, treatment of **dry eye** disease and corneal injury. Pharmaceutical formulations and methods of making the same are also disclosed. Methods of administering the same would include: topical administration via a liquid, gel, cream, or as part of a contact lens or selective release membrane; or systemic administration via nasal drops or spray, inhalation by nebulizer or other device, oral form (liquid or pill), injectable, intra-operative instillation or suppository form.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 111648-11-4 211427-08-6 401618-87-9

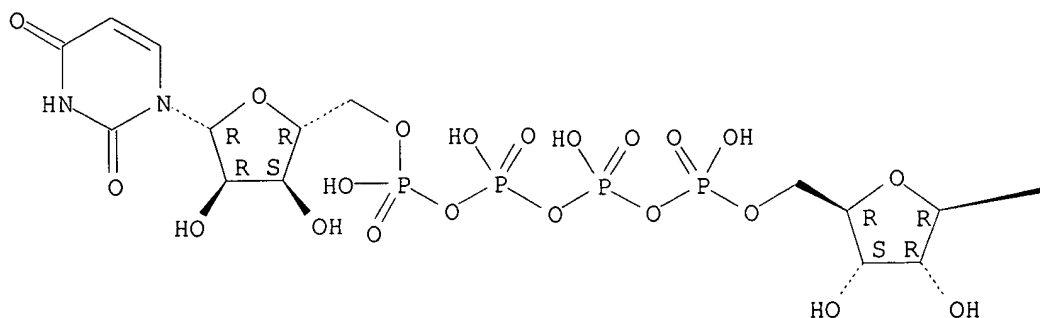
(method of treating dry eye disease with purinergic receptor agonists such as dinucleotides)

RN 111648-11-4 USPATFULL

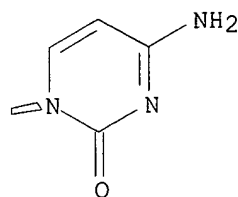
CN Uridine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with cytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



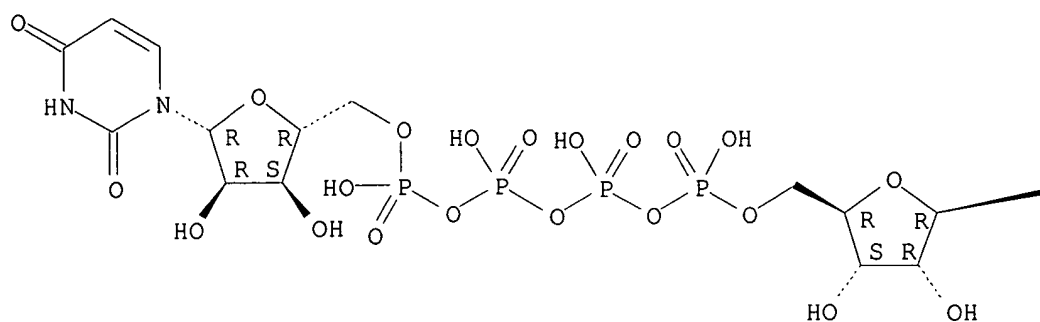
PAGE 1-B



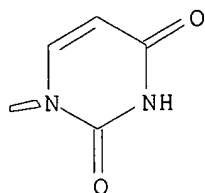
RN 211427-08-6 USPATFULL

CN Uridine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with uridine, tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

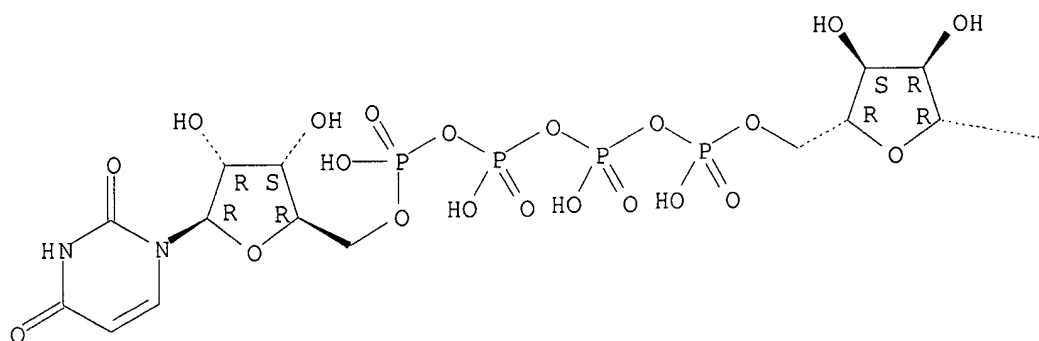


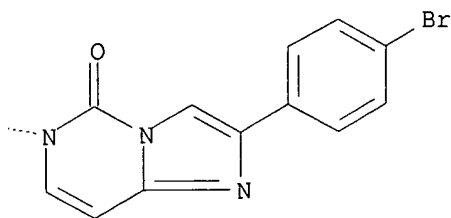
● 4 Na



RN 401618-87-9 USPATFULL  
 CN Uridine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with  
 2-(4-bromophenyl)-6-.beta.-D-ribofuranosylimidazo[1,2-c]pyrimidin-5(6H)-  
 one (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L6 ANSWER 5 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2002:192086 USPATFULL

TITLE: Method of treating **dry eye** disease  
with purinergic receptor agonists

INVENTOR(S): Yerxa, Benjamin R., Raleigh, NC, UNITED STATES  
Jacobus, Karla M., Cary, NC, UNITED STATES  
Pendergast, William, Durham, NC, UNITED STATES  
Rideout, Janet L., Raleigh, NC, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002103157	A1	20020801
APPLICATION INFO.:	US 2002-41826	A1	20020103 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-171169, filed on 14 Oct 1998, PENDING A 371 of International Ser. No. WO 1998-US2701, filed on 6 Feb 1998, UNKNOWN A 371 of International Ser. No. US 1997-797472, filed on 6 Feb 1997, PATENTED		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	HOWREY SIMON ARNOLD & WHITE, LLP, BOX 34, 301 RAVENSWOOD AVE., MENLO PARK, CA, 94025		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Page(s)		
LINE COUNT:	980		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and preparation for the stimulation of tear secretion in a subject in need of such treatment is disclosed. The method comprises administering to the ocular surfaces of the subject a purinergic receptor agonist such as uridine 5'-triphosphate (UTP), dinucleotides, cytidine 5'-triphosphate (CTP), adenosine 5'-triphosphate (ATP), or their therapeutically useful analogs and derivatives, in an amount effective to stimulate tear fluid secretion and enhance drainage of the **lacrimal** system. Pharmaceutical formulations and methods of making the same are also disclosed. Methods of administering the same would include: topical administration via a liquid, gel, cream, or as part of a contact lens or selective release membrane; or systemic administration via nasal drops or spray, inhalation by nebulizer or other device, oral form (liquid or pill), injectable, intra-operative instillation or suppository form.

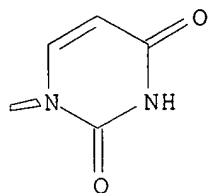
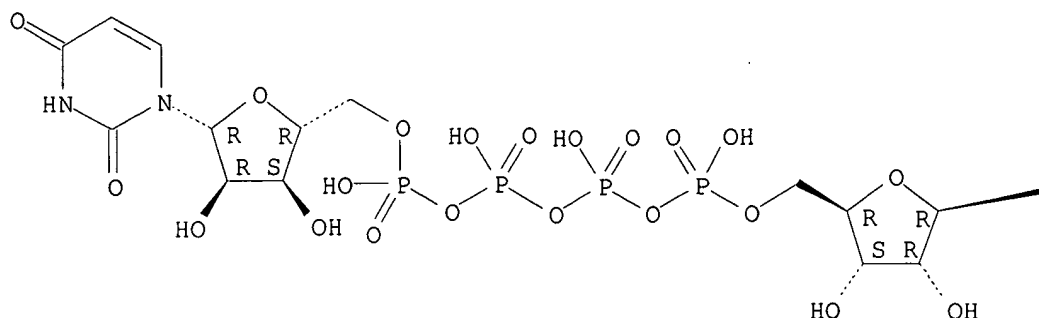
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **59985-21-6**, P1,P4-Diuridine 5'-tetraphosphate  
(uridine triphosphates and related compds. for treating ciliary dyskinesia)

RN 59985-21-6 USPATFULL

CN Uridine 5'-(pentahydrogen tetraphosphate), P'''.fwdarw.5'-ester with uridine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2002:157807 USPATFULL

TITLE: Certain dinucleotides and their use as modulators of mucociliary clearance and ciliary beat frequency

INVENTOR(S): Pendergast, William, Durham, NC, UNITED STATES

Yerxa, Benjamin R., Raleigh, NC, UNITED STATES

Rideout, Janet L., Raleigh, NC, UNITED STATES

Siddiqi, Suhaib M., Raleigh, NC, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002082417	A1	20020627
APPLICATION INFO.:	US 2001-7451	A1	20011106 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-101395, filed on 10 Jul 1998, PATENTED A 371 of International Ser. No. WO 1998-US2702, filed on 6 Feb 1998, UNKNOWN		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	HOWREY SIMON ARNOLD & WHITE, LLP, BOX 34, 301 RAVENSWOOD AVE., MENLO PARK, CA, 94025		
NUMBER OF CLAIMS:	11		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1201		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to certain novel dinucleotides and formulations thereof which are highly selective agonists of the P2Y.sub.2 and/or P2Y.sub.4 purinergic receptor. They are useful in the treatment of chronic obstructive pulmonary diseases such as chronic bronchitis, PCD, cystic fibrosis, as well as prevention of pneumonia due to immobility. Furthermore, because of their general ability to clear retained mucus secretions and stimulate ciliary beat frequency, the compounds of the present invention are also useful in the treatment of

sinusitis, otitis media and nasolacrimal duct obstruction. They are also useful for treatment of **dry eye** disease and retinal detachment as well as facilitating sputum induction and expectoration.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 59985-21-6, P1,P4-Diuridine 5'-tetrphosphate

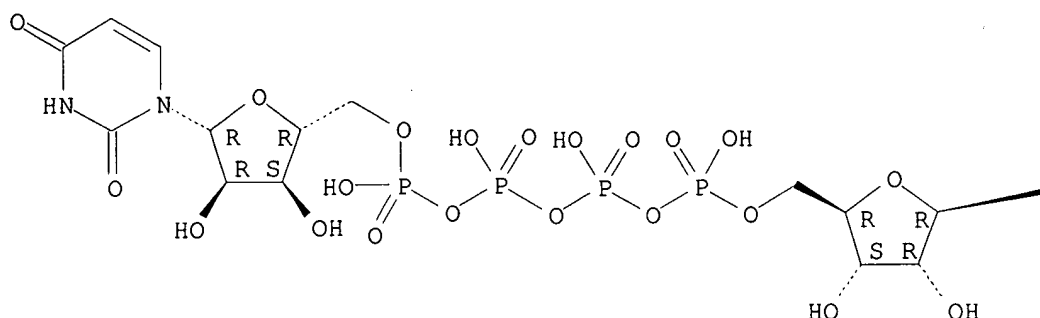
(uridine triphosphates and related compds. for treating ciliary dyskinesia)

RN 59985-21-6 USPATFULL

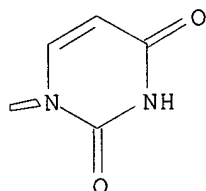
CN Uridine 5'-(pentahydrogen tetrphosphate), P'''.fwdarw.5'-ester with uridine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L6 ANSWER 7 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2002:126727 USPATFULL

TITLE: Method of treating **dry eye** disease with purinergic receptor agonists

INVENTOR(S): Yerxa, Benjamin R., Raleigh, NC, UNITED STATES  
Jacobus, Karla M., Cary, NC, UNITED STATES  
Pendergast, William, Durham, NC, UNITED STATES  
Rideout, Janet L., Raleigh, NC, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002065244	A1	20020530
APPLICATION INFO.:	US 2001-10055	A1	20011109 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-171169, filed on 14 Oct 1998, PENDING A 371 of International Ser. No. WO 1998-US2701, filed on 6 Feb 1998, UNKNOWN A 371 of International Ser. No. US 1997-797472, filed on 6 Feb 1997, PATENTED		
DOCUMENT TYPE:	Utility		

FILE SEGMENT: APPLICATION  
 LEGAL REPRESENTATIVE: HOWREY SIMON ARNOLD & WHITE, LLP, BOX 34, 301  
 RAVENSWOOD AVE., MENLO PARK, CA, 94025  
 NUMBER OF CLAIMS: 12  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 2 Drawing Page(s)  
 LINE COUNT: 981  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and preparation for the stimulation of tear secretion in a subject in need of such treatment is disclosed. The method comprises administering to the ocular surfaces of the subject a purinergic receptor agonist such as uridine 5'-triphosphate (UTP), dinucleotides, cytidine 5'-triphosphate (CTP), adenosine 5'-triphosphate (ATP), or their therapeutically useful analogs and derivatives, in an amount effective to stimulate tear fluid secretion and enhance drainage of the **lacrimal** system. Pharmaceutical formulations and methods of making the same are also disclosed. Methods of administering the same would include: topical administration via a liquid, gel, cream, or as part of a contact lens or selective release membrane; or systemic administration via nasal drops or spray, inhalation by nebulizer or other device, oral form (liquid or pill), injectable, intra-operative instillation or suppository form.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

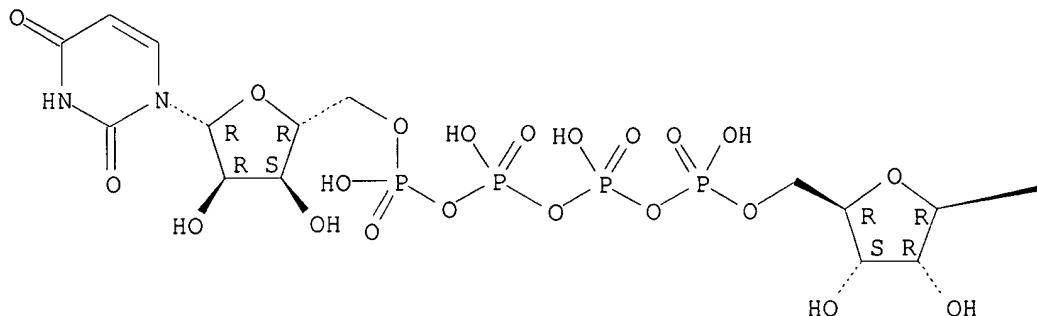
IT 59985-21-6, P1,P4-Diuridine 5'-tetrphosphate  
 (uridine triphosphates and related compds. for treating ciliary dyskinesia)

RN 59985-21-6 USPATFULL

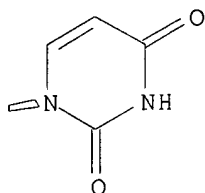
CN Uridine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with uridine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L6 ANSWER 8 OF 9 USPATFULL on STN

ACCESSION NUMBER: 2002:34549 USPATFULL

TITLE: Certain dinucleotides and their use as modulators of

INVENTOR(S): mucociliary clearance and ciliary beat frequency

Pendergast, William, Durham, NC, United States

Yerxa, Benjamin R., Raleigh, NC, United States

Rideout, Janet L., Raleigh, NC, United States

Siddiqi, Suhaib M., Raleigh, NC, United States

PATENT ASSIGNEE(S): Inspire Pharmaceuticals, Inc., Durham, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6348589	B1	20020219
	WO 9834942		19980813
APPLICATION INFO.:	US 1998-101395		19980710 (9)
	WO 1998-US2702		19980206
			19980713 PCT 371 date
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-798508, filed on 10 Feb 1997, now patented, Pat. No. US 5900407		
	Continuation-in-part of Ser. No. US 1997-797472, filed on 6 Feb 1997		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Geist, Gary		
ASSISTANT EXAMINER:	Owens, Howard V.		
LEGAL REPRESENTATIVE:	Halluin, Albert P., Kung, Viola T., Howrey Simon Arnold & White, LLP		
NUMBER OF CLAIMS:	9		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	1358		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to certain novel dinucleotides and formulations thereof which are highly selective agonists of the P2Y.sub.2 and/or P2Y.sub.4 purinergic receptor. They are useful in the treatment of chronic obstructive pulmonary diseases such as chronic bronchitis, PCD, cystic fibrosis, as well as prevention of pneumonia due to immobility. Furthermore, because of their general ability to clear retained mucus secretions and stimulate ciliary beat frequency, the compounds of the present invention are also useful in the treatment of sinusitis, otitis media and nasolacrimal duct obstruction. They are also useful for treatment of **dry eye** disease and retinal detachment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 59985-21-6P 111035-55-3P 111648-11-4P  
211427-11-1P 211448-72-5P 211448-76-9P  
211495-45-3P 211495-47-5P

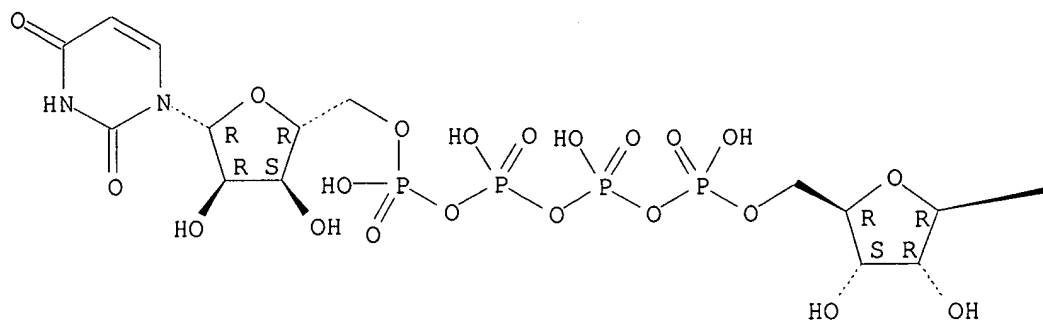
(prepn. of dinucleotides and their use as modulators of mucociliary clearance and ciliary beat frequency)

RN 59985-21-6 USPATFULL

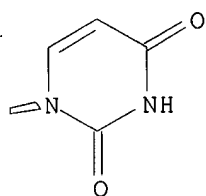
CN Uridine 5'-(pentahydrogen tetraphosphate), P''''.fwdarw.5'-ester with uridine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



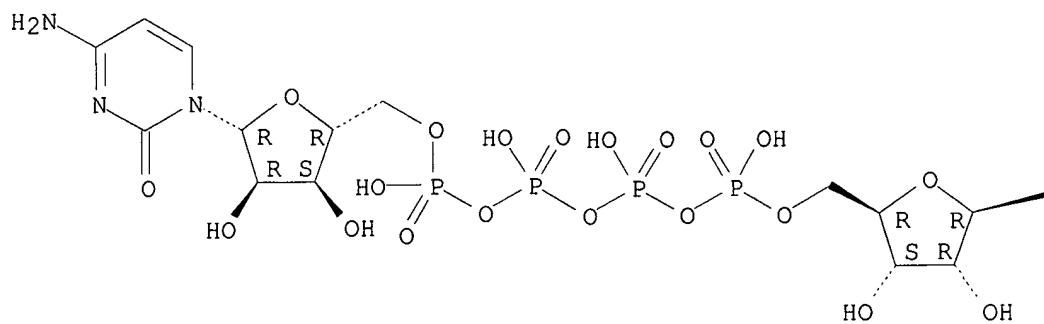
PAGE 1-B



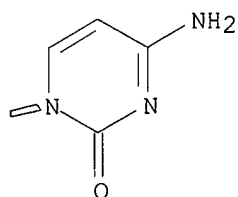
RN 111035-55-3 USPATFULL  
CN Cytidine 5'-(pentahydrogen tetrphosphate), P'''-fwdarw.5'-ester with  
cytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

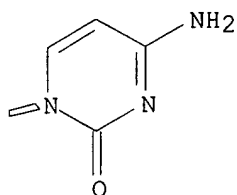


PAGE 1-B





PAGE 1-B

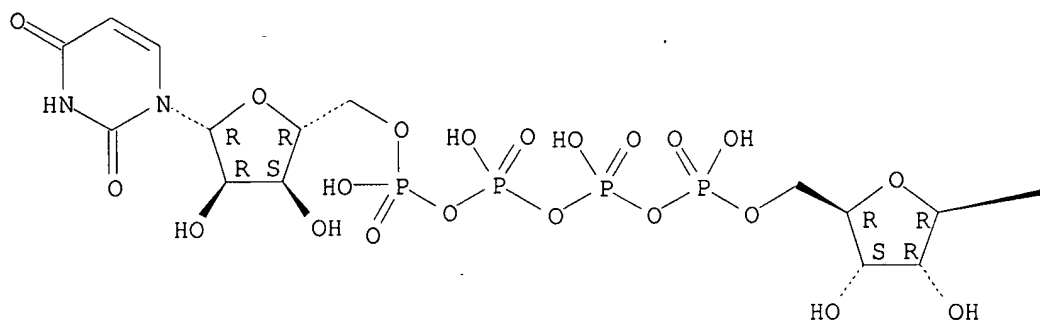


RN 111648-11-4 USPATFULL

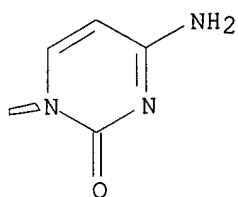
CN Uridine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with  
cytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

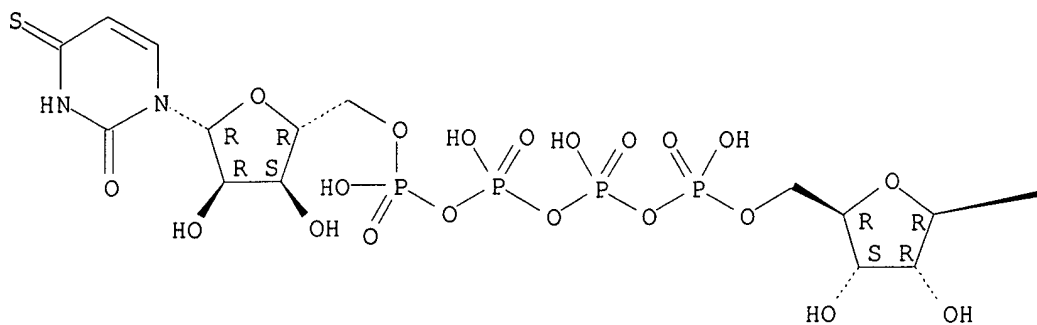


RN 211427-11-1 USPATFULL

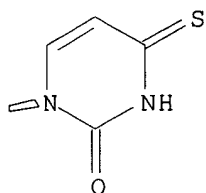
CN Uridine 5'-(pentahydrogen tetraphosphate), 4-thio-, P'''-fwdarw.5'-ester  
with 4-thiouridine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



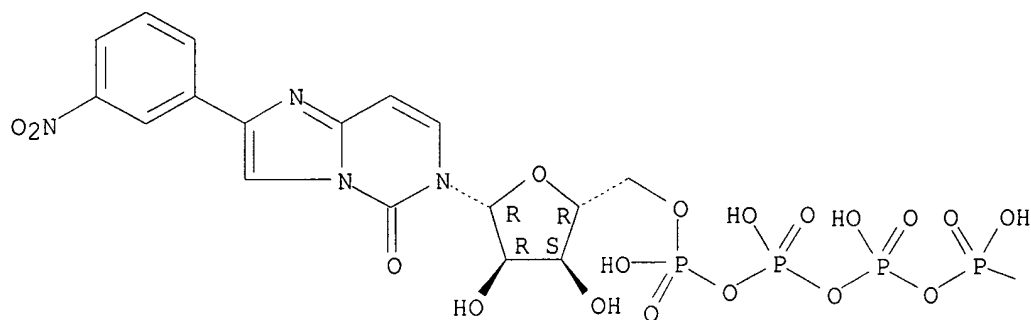
PAGE 1-B



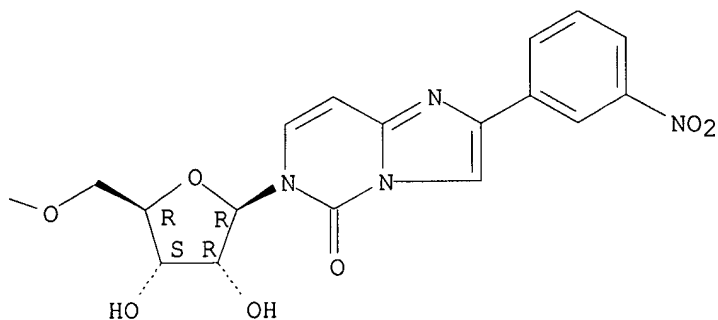
RN 211448-72-5 USPATFULL  
CN Imidazo[1,2-c]pyrimidin-5(6H)-one, 6-[5-O-[hydroxy[[hydroxy[[hydroxy(phosphonoxy)phosphinyl]oxy]phosphinyl]oxy]phosphinyl]-.beta.-D-ribofuranosyl]-2-(3-nitrophenyl)-, P''''.fwdarw.5'-ester with 2-(3-nitrophenyl)-6-.beta.-D-ribofuranosylimidazo[1,2-c]pyrimidin-5(6H)-one, tetraammonium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



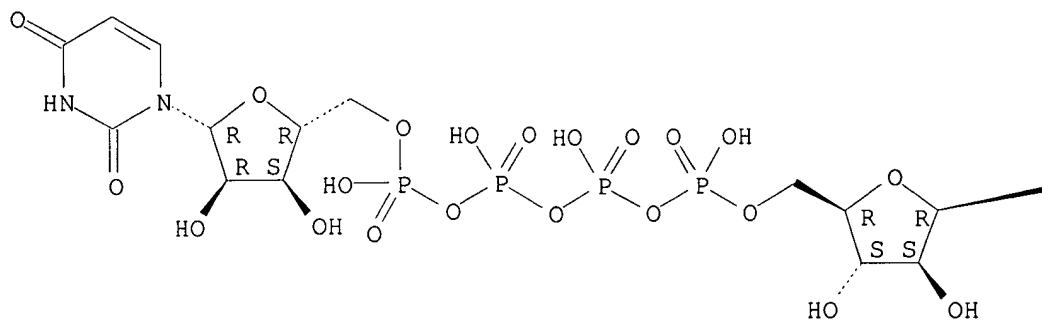
PAGE 1-B



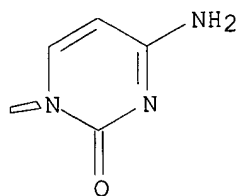
RN 211448-76-9 USPATFULL  
CN Uridine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with  
4-amino-1-.beta.-D-arabinofuranosyl-2(1H)-pyrimidinone (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



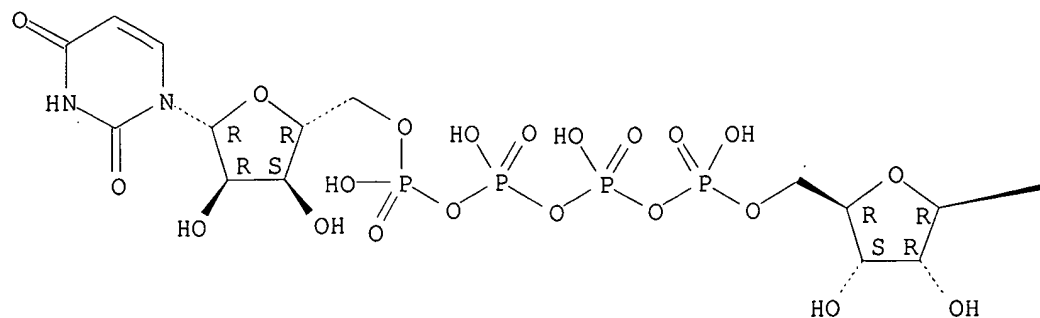
RN 211495-45-3 USPATFULL  
CN Uridine 5'-(pentahydrogen tetraphosphate), 2'(or 3')-benzoate,  
P'''-fwdarw.5'-ester with uridine (9CI) (CA INDEX NAME)

CM 1

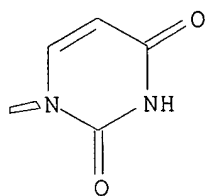
CRN 59985-21-6  
CMF C18 H26 N4 O23 P4  
CDES 5:B-D-RIBO,B-D-RIBO

Absolute stereochemistry.

PAGE 1-A

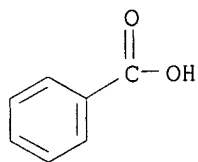


PAGE 1-B



CM 2

CRN 65-85-0  
CMF C7 H6 O2



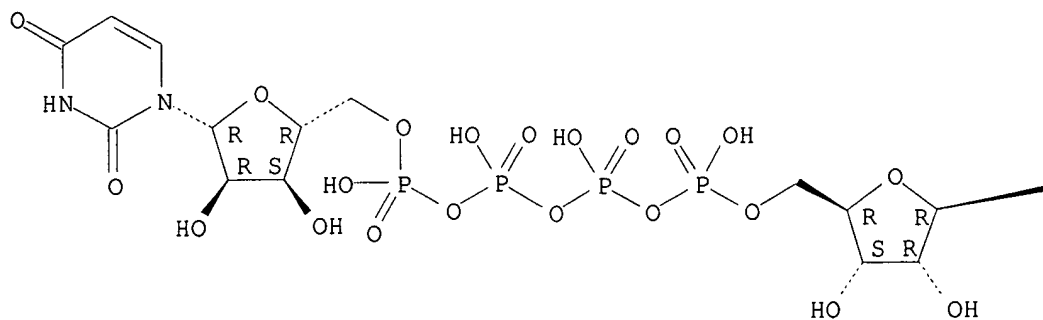
RN 211495-47-5 USPATFULL  
CN Uridine 5'-(pentahydrogen tetraphosphate), 2'(or 3')-benzoate,  
P'''-fwdarw.5'-ester with uridine 2'(or 3')-benzoate (9CI) (CA INDEX  
NAME)

CM 1

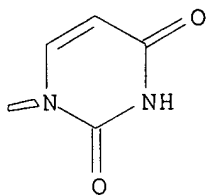
CRN 59985-21-6  
CMF C18 H26 N4 O23 P4  
CDES 5:B-D-RIBO,B-D-RIBO

Absolute stereochemistry.

PAGE 1-A

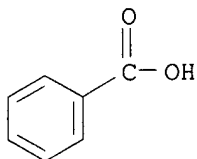


PAGE 1-B



CM 2

CRN 65-85-0  
CMF C7 H6 O2



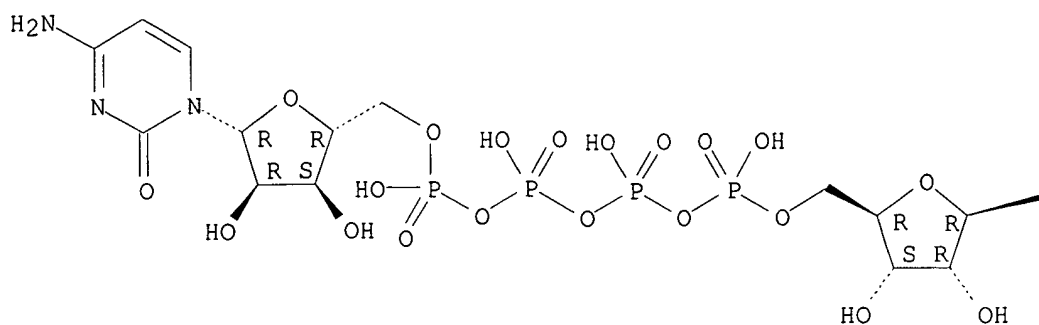
IT 211448-71-4

(prepn. of dinucleotides and their use as modulators of mucociliary clearance and ciliary beat frequency)

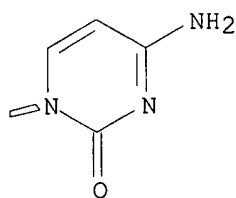
RN 211448-71-4 USPATFULL

CN Cytidine 5'-(pentahydrogen tetraphosphate), P'''-fwdarw.5'-ester with cytidine, tetraammonium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 4 NH<sub>3</sub>



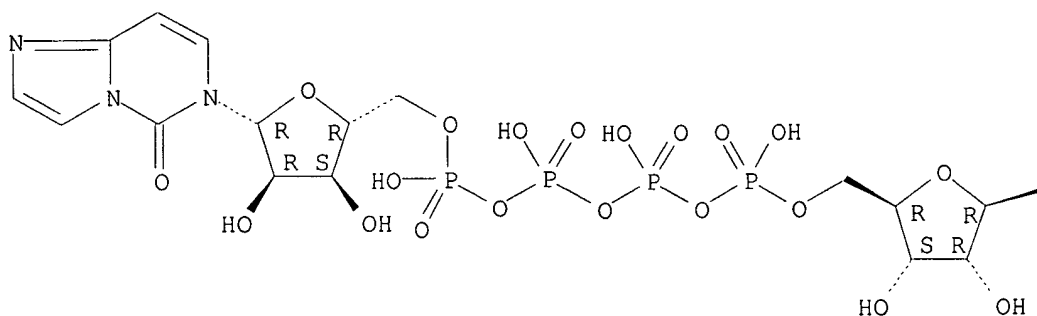
IT 211427-07-5P 211448-75-8P

(prepn. of dinucleotides and their use as modulators of mucociliary clearance and ciliary beat frequency)

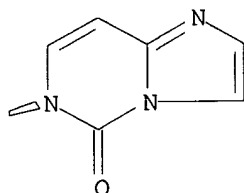
RN 211427-07-5 USPATFULL

CN Imidazo[1,2-c]pyrimidin-5(6H)-one, 6-[5-O-[hydroxy[[hydroxy[[hydroxy(phosphonoxy)phosphinyl]oxy]phosphinyl]oxy]phosphinyl]-.beta.-D-ribofuranosyl]-, P'''-fwdarw.5'-ester with 6-.beta.-D-ribofuranosylimidazo[1,2-c]pyrimidin-5(6H)-one (9CI) (CA INDEX NAME)

Absolute stereochemistry.



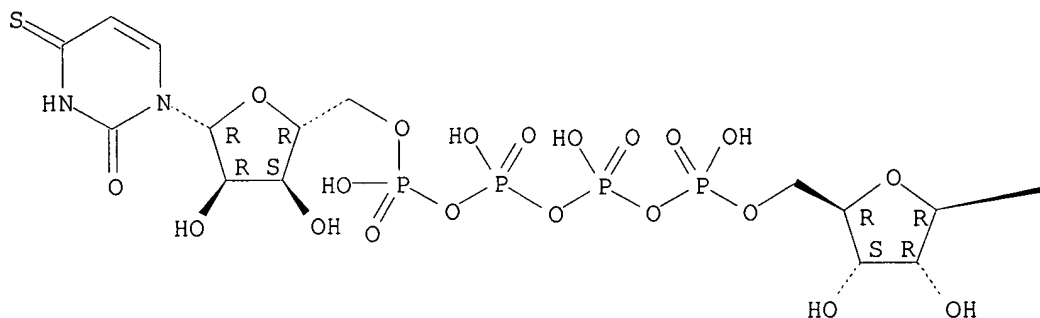
PAGE 1-B



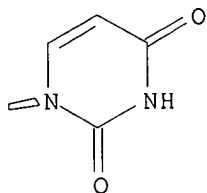
RN 211448-75-8 USPATFULL  
CN Uridine 5'-(pentahydrogen tetraphosphate), 4-thio-, P'''-fwdarw.5'-ester  
with uridine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L6 ANSWER 9 OF 9 USPATFULL on STN  
ACCESSION NUMBER: 1999:53618 USPATFULL  
TITLE: Method of treating **dry eye** disease  
with uridine triphosphates and related compounds  
INVENTOR(S): Yerxa, Benjamin R., Raleigh, NC, United States  
Jacobus, Karla M., Cary, NC, United States  
Pendergast, William, Durham, NC, United States  
Rideout, Janet L., Raleigh, NC, United States  
PATENT ASSIGNEE(S): Inspire Pharmaceuticals, Inc., Durham, NC, United States (U.S. corporation)

NUMBER KIND DATE

-----

PATENT INFORMATION: US 5900407 19990504  
 APPLICATION INFO.: US 1997-797472 19970206 (8)  
 DOCUMENT TYPE: Utility  
 FILE SEGMENT: Granted  
 PRIMARY EXAMINER: Fay, Zohreh  
 LEGAL REPRESENTATIVE: Halluin, Albert P., Bendrick, John A. Howrey & Simon  
 NUMBER OF CLAIMS: 9  
 EXEMPLARY CLAIM: 1  
 LINE COUNT: 719

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and preparation for the stimulation of tear secretion in a subject in need of such treatment is disclosed. The method comprises administering to the ocular surfaces of the subject a purinergic receptor agonist such as uridine 5'-triphosphate [UTP], dinucleotides, cytidine 5'-triphosphate [CTP], adenosine 5'-triphosphate [ATP], or their therapeutically useful analogs and derivatives, in an amount effective to stimulate tear fluid secretion. Pharmaceutical formulations and methods of making the same are also disclosed. Methods of administering the same would include: topical administration via a liquid, gel, cream, or as part of a contact lens or selective release membrane; or systemic administration via nasal drops or spray, inhalation by nebulizer or other device, oral form (liquid or pill), injectable, intra-operative instillation or suppository form.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 59985-21-6, P1,P4-Diuridine 5'-tetrphosphate

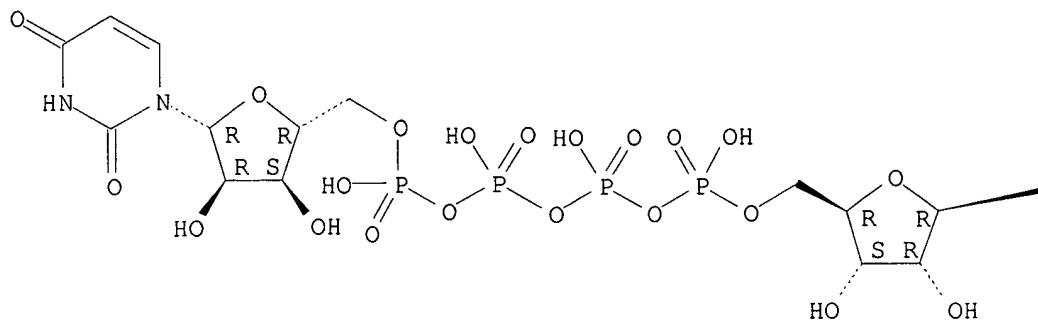
(uridine triphosphates and related compds. for treating ciliary dyskinesia)

RN 59985-21-6 USPATFULL

CN Uridine 5'-(pentahydrogen tetrphosphate), P''''.fwdarw.5'-ester with uridine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

